IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

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| Applicant | : Reiko Irie et al. | Art Unit | : 1645 |
| Serial No. | : 10/564,665 | Examiner | : Unknown |
| Filed | : September 21, 2006 | Conf. No. | : 1468 |

Title : IGM PRODUCTION BY TRANSFORMED CELL AND METHOD OF QUANTIFYING THE SAME

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

RESPONSE TO NOTICE OF DEFECTIVE RESPONSE

Applicants are in receipt of a Notice of Defective Response mailed February 13, 2008, requesting payment of additional claims fees. It is believed this Notice was sent in error. Applicants filed a Preliminary Amendment and the appropriate excess claims fee of $3,500 with the application on September 21, 2006. See the copy of the Preliminary Amendment attached hereto as Exhibit A. That Preliminary Amendment is not listed on the Notification as part of the record, so appears to have been overlooked by the Office when the claim fees were calculated.

Applicants submit that the Response was complete and timely filed and request that the Notice be withdrawn and the filing date of September 21, 2006, be granted.

Please apply any charges or credits to Deposit Account No. 06-1050, referencing the attorney docket number shown above.

Respectfully submitted,

Date: March 11, 2008

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# EXHIBIT A

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

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| Applicant | : Reiko Irie et al. | Art Unit | : Unknown |
| Serial No. | : 10/564,665 | Examiner | : Unknown |
| Filed | : January 13, 2006 | Conf. No. | : 1468 |
| Title | : IGM PRODUCTION BY TRANSFORMED CELL AND METHOD OF QUANTIFYING THE SAME | | |

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

PRELIMINARY AMENDMENT

Prior to examination, please amend the application as indicated on the following pages.

Amendments to the Specification:

Please amend the title to read as:

IgM PRODUCTION BY TRANSFORMED CELLS AND METHODS FOR QUANTIFYING SAID IgM PRODUCTION

Amendments to the Claims:

This listing of claims replaces all prior versions and listings of claims in the application:

Listing of Claims:

1. (Currently Amended) A transformed cell producing IgM of a) 100 mg/L or more; or b) 35 pg/cell/day or more.

2. (Canceled)

3. (Currently Amended) The transformed cell of claim 1 ~~or 2~~, which is a eukaryotic cell.

4. (Currently Amended) The transformed cell of claim 1 ~~or 2~~, which is a prokaryotic cell.

5. (Original) The transformed cell of claim 3, which is a mammalian cell.

6. (Currently Amended) The transformed cell of claim 1 ~~any one of claims 1 to 5~~, which is an established cell line.

7. (Original) The transformed cell of claim 6, which is a non-lymphoid cell line.

8. (Original) The transformed cell of claim 7, which is a CHO cell line.

9. (Original) An expression vector comprising both (1) a nucleotide sequence encoding an IgM H chain and (2) a nucleotide sequence encoding an IgM L chain in the same vector, or a gene fragment comprising the genes (1) and (2).

10. (Currently Amended) The expression vector of claim 9, wherein the vector comprises ~~An expression vector comprising (1) a nucleotide sequence encoding an IgM H chain, (2) a nucleotide sequence encoding an IgM L chain, and~~ (3) a nucleotide sequence encoding an IgM J chain in the same vector, or a gene fragment comprising the genes (1), (2), and (3).

11. (Currently Amended) The expression vector or gene fragment of claim ~~9 or 10~~, wherein IgM secretion is controlled by a transcriptional regulatory sequence.

12. (Original) The expression vector or gene fragment of claim 11, wherein the transcriptional regulatory sequence is selected from the group consisting of:

- major late promoter of adenovirus 2;
- early promoter of simian virus 40;
- mouse mammary tumor virus (MMTV)-LTR promoter;
- thymidine kinase promoter of herpes simplex virus;
- cytomegalovirus promoter;
- polypeptide chain elongation factor 1 α promoter;
- bovine growth hormone promoter;
- β actin gene promoter; and
- CAG promoter.

13. (Original) The expression vector or gene fragment of claim 12, wherein the transcriptional regulatory sequence is selected from the group consisting of:

- early promoter of simian virus 40;
- cytomegalovirus promoter;

- polypeptide chain elongation factor 1 α promoter; and
- CAG promoter.

14. (Currently Amended) A transformed cell transformed by the vector or gene fragment of claim 9 ~~any one of claims 9 to 13~~.

15. (Canceled)

16. (Currently Amended) The transformed cell of claim 14 ~~or 15~~, wherein the expression vector or gene fragment comprises a nucleotide sequence encoding a J chain.

17. (Currently Amended) The transformed cell of claim 14 ~~any one of claims 14 to 16~~, wherein the vector or gene fragment comprises a nucleotide sequence encoding an IgM J chain and the cell produces pentamer IgM with a content of 60% or more.

18. (Original) The transformed cell of claim 17, which produces pentamer IgM with a content of 80% or more.

19. (Currently Amended) The transformed cell of claim 14 ~~or 15~~, wherein the vector or gene fragment comprises no nucleotide sequence encoding an IgM J chain and the cell produces hexamer IgM with a content of 50% or more.

20. (Original) The transformed cell of claim 19, which produces hexamer IgM with a content of 80% or more.

21. (Currently Amended) The transformed cell of claim 14 ~~any one of claims 14 to 16~~, wherein the vector or gene fragment comprises a nucleotide sequence encoding an IgM J chain

and the cell produces IgM for which the ratio of the produced pentamer and hexamer (pentamer/hexamer ratio) is 1.5 or more.

22. (Currently Amended) The transformed cell of claim 14 ~~or 15~~, wherein the vector or gene fragment comprises no nucleotide sequence encoding an IgM J chain and the cell produces IgM for which the ratio of the produced hexamer and pentamer (hexamer/pentamer ratio) is 1.5 or more.

23. (Currently Amended) The transformed cell of claim 14 ~~or 15~~, wherein the expression vector or gene fragment comprising a gene encoding IgM H and L chains comprises no nucleotide sequence encoding a J chain and the nucleotide sequence encoding the J chain has been expressively introduced by co-transfection.

24. (Currently Amended) A method for producing an IgM, comprising a step of culturing the cell of claim 1 ~~any one of claims 1 to 8 and 14 to 23~~ and then collecting the IgM.

25. (Currently Amended) A method for producing a substantially pure IgM, comprising a step of purifying an IgM from a culture supernatant obtained from culture of the cell of claim 1 ~~any one of claims 1 to 8 and 14 to 23~~.

26. (Original) An IgM obtained by the method of claim 24.

27. (Original) A substantially pure IgM obtained by the method of claim 25.

28. (Currently Amended) The IgM of claim 26 ~~or 27~~, which is a human, mouse, human chimeric, or humanized antibody.

29. (Currently Amended) The IgM of claim 26 ~~any one of claims 26 to 28~~, which is a substantially pure pentamer or hexamer.

30. (Original) A substantially pure pentamer or hexamer IgM comprising a sugar chain added by a CHO cell.

31. (Currently Amended) The IgM of claim 26 ~~any one of claims 26 to 30~~, which is an anti-sugar chain antibody.

32. (Original) The IgM of claim 31, which is an anti-ganglioside antibody.

33. (Original) The IgM of claim 32, which is an anti-GM2 or GM3 antibody.

34. (Currently Amended) An isolated polynucleotide comprising:

a) the nucleotide sequence of SEQ ID NO: 1 or a nucleotide sequence encoding the amino acid sequence of SEQ ID NO: 2;

b) the nucleotide sequence of SEQ ID NO: 3 or a nucleotide sequence encoding the amino acid sequence of SEQ ID NO: 4;

c) the nucleotide sequence of SEQ ID NO: 19 or a nucleotide sequence encoding the amino acid sequence of SEQ ID NO: 20; or

d) the nucleotide sequence of SEQ ID NO: 21 or a nucleotide sequence encoding the amino acid sequence of SEQ ID NO: 22.

35. (Canceled)

36. (Original) An isolated protein comprising an amino acid sequence encoded by the polynucleotide of claim 34.

37. (Canceled)

38. (Currently Amended) An IgM comprising one or more proteins of claim 36 ~~the protein of claim 36 and the protein of claim 37 as constituent units~~.

39. (Original) The IgM of claim 38, further comprising an IgM J chain.

40. (Original) The IgM of claim 39, which is a pentamer.

41-47. (Canceled)

48. (Currently Amended) A pharmaceutical composition comprising the IgM of claim 26 ~~any one of claims 26 to 33, 38, and 45~~.

49. (Original) A pharmaceutical composition comprising 80% or more pentamer IgM.

50. (Original) A pharmaceutical composition comprising 50% or more hexamer IgM.

51. (Original) The pharmaceutical composition of claim 50, comprising 80% or more hexamer IgM.

52. (Original) A pharmaceutical composition comprising an IgM for which pentamer/hexamer ratio is 1.5 or more.

53. (Original) A pharmaceutical composition comprising an IgM for which hexamer/pentamer ratio is 1.5 or more.

54. (Original) A method for analyzing an IgM polymer, comprising a step of separating an IgM by SDS-polyacrylamide gel electrophoresis using as a carrier polyacrylamide gel satisfying at least one condition selected from the group consisting of:

a) a polyacrylamide gel polymerized at a high temperature;

b) a polyacrylamide gel containing a high concentration of ammonium persulfate and glycerol; and

c) a polyacrylamide gel homogenized by stirring and degassed prior to polymerization.

55. (Original) The method of claim 54, wherein the temperature in condition a) is 37°C or higher.

56. (Original) The method of claim 54, wherein the concentration of ammonium persulfate in condition b) is 0.25% or more.

57. (Original) The method of claim 54, wherein the polyacrylamide gel satisfies at lease two conditions selected from the group consisting of conditions a) to c).

58. (Original) The method of claim 54, wherein the polyacrylamide gel satisfies all the conditions a) to c).

59. (Original) The method of claim 54, wherein a buffer for electrophoresis is a Tris-acetate SDS electrophoresis buffer.

60. (Original) The method of claim 54, wherein the IgM polymer is an IgM pentamer and/or hexamer.

61. (Original) The method of claim 54, wherein the method comprises analyzing an IgM aggregate.

62. (Original) The method of claim 54, wherein the method is free from use of RI.

63. (Original) The method of claim 54, comprising a step of quantifying the IgM polymer separated after electrophoresis.

64. (Original) An electrophoresis gel for separating an IgM polymer by SDS-polyacrylamide gel electrophoresis, comprising a polyacrylamide gel satisfying at least one condition selected from the group consisting of:

a) a polyacrylamide gel polymerized at a high temperature;

b) a polyacrylamide gel containing a high concentration of ammonium persulfate and glycerol; and

c) a polyacrylamide gel homogenized by stirring and degassed prior to polymerization.

65. (Original) A method for producing an electrophoresis gel for separating an IgM polymer by SDS-polyacrylamide gel electrophoresis, comprising at least one step selected from the group consisting of:

a) polymerizing an acrylamide at a high temperature;

b) adding a high concentration of ammonium persulfate to an acrylamide, and

c) homogenizing an acrylamide by stirring and degassed prior to polymerization.

66. (New) A method for producing an IgM, comprising a step of culturing the cell of claim 14 and then collecting the IgM.

67. (New) A method for producing a substantially pure IgM, comprising a step of purifying an IgM from a culture supernatant obtained from culture of the cell of claim 14.

68. (New) A pharmaceutical composition comprising the IgM of claim 30.

69. (New) A pharmaceutical composition comprising the IgM of claim 38.

## REMARKS

Following entry of the above amendment, claims 1, 3-14, 16-34, 36, 38-40, and 48-69 will be pending in this application. Claims 1, 3, 4, 6, 10, 11, 14, 16, 17, 19, 21-25, 28, 29, 31, 34, and 38 have been amended, claims 2, 15, 35, 37, and 41-47 have been canceled, and new claims 66-69 have been added. Support for the amendments to the claims can be found throughout the specification and claims as originally filed. No new matter has been added. Applicants ask that all claims be examined in view of the amendments to the claims.

The amendment to the specification updates the title. No new matter has been added.

Please apply the excess claims fee of $3,500, the Petition for Extension of Time fee of $2,160, and any other charges or credits to Deposit Account No. 06-1050, referencing Attorney Docket No. 14875-155US1.

Respectfully submitted,

Date: Sept. 20, 2006

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